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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/062,375	01/30/2002	J. Gregor Sutcliffe	22908-0002 C1	3744

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EXAMINER	
HAYES, ROBERT CLINTON	
ART UNIT	**PAPER NUMBER**
1647	

DATE MAILED: 01/21/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/062,375	SUTCLIFFE ET AL.	
	Examiner	Art Unit	
	Robert C. Hayes, Ph.D.	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *02 November 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date ____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *reference from 892*.

DETAILED ACTION

Response to Amendment

1. The amendment filed 11/02/04 has been entered.

2. The rejection of claims 21-23 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-4 of U.S. Patent No. 6,479,642 B1 is withdrawn due to the submission of a terminal disclaimer.

3. The rejection of claims 21-23 under 35 U.S.C. 112, second paragraph, as being indefinite is withdrawn due to the amendment of the claims. It is again suggested that amending claim 23 to "... which induces cortical slow-wave sleep isoform two" would be more grammatically correct.

4. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

5. Applicants' arguments filed 11/02/04 have been considered but are not found persuasive.

6. Claim 22 stands rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for pharmaceutical compositions comprising the specific isolated and purified cortistatin polypeptides of SEQ ID NO: 26, or structurally and functionally defined

fragments thereof, does not reasonably provide enablement for any biological functional equivalent proteins with no defined structural characteristics. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims, for the reasons made of record in Paper No: 20040818, and as follows.

Applicants argue on pages 6-8 of the response that "the priority of the instant invention goes back to 1996 at which time the state of the art had already progressed to understanding the importance of conserved protein sequences across species, and cites Sekido et al who found that there was 78% identity between chicken and mouse delta EF1, *In re* Certain Limited, and *Massachusetts Institute of Technology v. A. B. Fortia*. In contrast to Applicants' assertions, the issue is that the specification alternatively teaches how to make allelic variants (i.e., as it relates to being 95% or 98 % identical to SEQ ID NO: 26, as described in the sentence bridging page 17 and 18 of the specification, which Applicants correctly recite), versus teaching how to make a protein with no base structure. The issue is also not whether sequences can be found to be related after-the-fact, as taught in Sekido, but whether or not the instant claims recite definable structural and functional characteristics, and whether the specification teaches which particular amino acids are critical for any cortistatin polypeptide's function, and how to structurally distinguish such from any different polypeptide sequence that possesses none of the desired functions of the instant invention, as previously made of record. In the instant case, only pharmaceutical compositions comprising biologically functional equivalent proteins are being claimed, and therefore, remain not enabled for the reasons previously made of record; consistent

with the teachings of Rudinger previously made of record. Further, in contrast to the teachings of Sekido et al., Skolnick et al. (2000) alternatively teach in their review article that:

"Sequence-based methods for functional prediction are inadequate because of the multifunctional nature of proteins. Proteins can gain and lose function during evolution and may, indeed, have multiple functions in the cell (Box 1). Sequence-to-function methods cannot specifically identify these complexities. Inaccurate use of sequence-to-function methods has led to significant function-annotation errors in the sequence databases". (e.g., see page 34).

Accordingly, it was held in *Ex parte Maizel* (27 USPQ2d 1662 at 1665 (BPAI 1992)) that:

> Appellants have not chosen to claim the DNA [product] by what it is but, rather, by what it does, i.e., encoding either a protein exhibiting certain characteristics, *or* a biologically functional equivalent thereof. Appellants' claims might be analogized to a single means claim of the type disparaged by the Court of Customs and Patent Appeals in *In re Hyatt,* 708F.2d 712, 218 USPQ 195 (Fed. Cir. 1983). The problem with the phrase "biologically functional equivalent thereof" is that it covers any conceivable means, i.e., cell or DNA, which achieves the stated biological result while the specification discloses, at most, only a specific DNA [product] segment known to the inventor. Clearly the disclosure is *not commensurate in scope with the claim*s [emphasis added].

Thus, in that no structure is recited in the claim, this claim encompasses pharmaceutical compositions comprising any "biologically functional equivalent" product, which therefore is not enabled, and for the reasons made of record.

7. Claims 21-23 stand rejected under 35 U.S.C. 102(a) as being anticipated by Fukusumi et al. (IDS REF #C2), for the reasons made of record in Paper No: 20040818, and as follows.

It is again noted that because no human cortistatin polypeptides were described in parent application no. 08/648,322 (now U.S. Patent 6,074,872), priority is held to be the filing date of parent application 08/857,389 (now U.S. Patent 6,479,642; filed 05/15/97).

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application); the disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35

U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

Applicants argue on pages 9-10 of the response that "U.S. Patent 6,074,872 (filed May 15, 1996) *does* teach human cortistatin", and cites three passages describing an invitation for others to isolate human cortistatin. However, in contrast to Applicants' assertions that '872 *"does* teach human cortistatin", nowhere in '872 is the sequence for human cortistatin disclosed, or is human cortistatin shown to be isolated. Not until U.S. Patent 6,479,642 (filed May 15, 1997) were any sequences for human cortistatin described (e.g., SEQ ID NO: 26), along with any pharmaceutical compositions comprising such. Therefore, Applicants' arguments are a misrepresentation of what '872 actually teaches, and therefore, are not persuasive.

In summary, Fukusumi et al. teach isolation and purification of human cortistatin of SEQ ID NO: 26 (pg. 158, Fig. 1) in pharmaceutical compositions (page 158, 1st col.) that include the pharmaceutically acceptable carrier, AcONH4 buffer (pH 8) and also comprise the pharmaceutically acceptable carrier, H2O, in dosages of between 10 pM and 1μM of cortistatin (Fig.4), as well as dosages of 0.1-1 nmol/ brain (Fig. 7 and page 162), which therefore are between about 50 *u*g to about 750 mg; thereby, meeting the limitations of claims 21-23.

8. The Declaration filed on 10/18/04 under 37 CFR 1.131 has been considered but is ineffective to overcome the Fukusumi et al reference. The evidence submitted is insufficient to establish a conception of the invention prior to the effective date of the Fukusumi et al reference, because no evidence has been submitted to establish a conception of the invention of any "pharmaceutical compositions" prior to the effective date of the reference, and because the putative human cortistatin protein itself was not isolated and purified in a pharmaceutical

composition within the enclosed "manuscript" (exhibit B) and/or laboratory note book entries (exhibit A & B) (i.e., no dosages, as claimed, were contemplated either). While conception is the mental part of the inventive act, it must be capable of proof, such as by demonstrative evidence or by a complete disclosure to another. Conception is more than a vague idea of how to solve a problem. The requisite means themselves and their interaction must also be comprehended. See *Mergenthaler v. Scudder*, 1897 C.D. 724, 81 O.G. 1417 (D.C. Cir. 1897).

Further, in contrast to Applicants' assertion on page 10 of the response that pharmaceutical compositions of human cortistatin were described in Exhibit A of the 1.131 declaration because "[t]he clones were precipitated with isopropanol and then ammonium hydroxide (NH4OH) and Ethanol (EtOH); and resuspended in H2O" after preparing standard minipreps using Qiagen columns, Qiagen columns are alternatively used to isolate DNA preps (i.e., "the clones"), not protein preps. DNA compositions are not protein compositions. Thus, Applicants' arguments are simply incorrect.

9. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Robert Hayes whose telephone number is (571) 272-0885. The examiner can normally be reached on Monday through Thursday, and alternate Fridays, from 8:30 AM to 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback, can be reached on (571) 272-0961. The fax phone number for this Group is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Robert C. Hayes, Ph.D.
January 18, 2005

ROBERT C. HAYES, PH.D.
PATENT EXAMINER